Should the severity of obesity affect our decision for heart transplant candidacy in pediatrics?

In this issue of the Journal, the article entitled "Obesity Class Does Not Further Stratify Outcome in Overweight and Obese Pediatric Patients After Heart Transplant" by Ryan et al. explores the relationship between overweight and obesity and long-term outcomes post-heart transplant among children and adolescents. In an analysis of a retrospective cohort derived from the United Network for Organ Sharing (UNOS) registry, the authors grade the severity of obesity using a 3-level obesity classification recently described by Skinner et al. By combining the overweight and obese classes, they were able to demonstrate that excess weight is an independent risk factor for death post-transplant (hazard ratio 1.244 [95% CI 1.097-1.411]). However, there was no significant difference observed in the post-transplant survival between overweight patients and those in any of the 3 classes of obesity in an unadjusted survival analysis. Given the small hazard ratio and the heterogeneity of the overweight and obese cohort, the authors were unable to draw a conclusion as to whether a strict body mass index (BMI) criteria could be used for heart transplant assessment.

The main strength of this article is their use of strict definitions for the overweight and obesity classes. Until recently, definitions of overweight and obesity among children and adolescents have been inconsistent in the literature. Lack of a universal definition has likely led to the observed variability of the effect of obesity on transplant outcomes. The authors also employed a strong analytic method to assess the effect of overweight and obesity on long-term outcomes, while taking into account other obesity-related risk factors and comorbidities.

The main limitation of this study was the insufficient number of patients in the higher classes of obesity (142 in class 2 obesity [121%-140% of 95th percentile of BMI], and 56 in class 3 obesity [>140% of the 95th percentile of BMI]), which prevented the authors from examining the 3 classes of obesity as independent variables in their multivariable regression analysis. Being underpowered is a frequent problem in pediatric research, and this issue is further compounded by the fact that 26% of patients (n = 1257) were excluded due to missing BMI status at the time of transplant listing.

The findings of this study highlight the need for improved understanding of the effect of obesity, but more specifically severe obesity, on transplant outcomes in children and adolescents. This issue is also brought forward by the current organ shortage and the need for better risk stratification at the time of transplant assessment. In addition, patients with obesity often experience stigma and discrimination, both by laypersons and health care professionals themselves, making the need for evidence-based justification of listing criteria even more important. Certainly, the increasing prevalence of overweight and obesity in children and adults is very concerning, and the rising rate of severe obesity brings new challenges and considerations for modern health care. Historically, criteria for adult heart transplantation included a very strict criterion for obesity (BMI >30 kg/m²) to serve as a guideline for transplant candidacy. However, more recent data in adult populations demonstrate unclear associations of obesity and outcomes post-heart transplant, and this is complicated further by the apparent obesity "paradox" seen among adult heart failure patients in whom overweight is actually associated with improved long-term outcomes. Given what we know about the problematic cardiometabolic effects of obesity and the associated comorbidities, it is hard to imagine that severe obesity would not have some impact on long-term outcome. Evidence suggests that increasing severity of obesity in children and adolescents is associated with higher risk of low HDL cholesterol levels, higher systolic and diastolic blood pressures, higher triglyceride levels, and higher glycated hemoglobin levels, which should consequently have an effect on long-term cardiovascular risk factors and survival post-transplant. However, due to the limitations noted above, this analysis was unable to demonstrate that severe obesity has a more significant impact on post-transplant outcomes.

The current obesity epidemic represents a serious public health problem. Because of its limitations, this study is unable to define a BMI criteria for lower risk pediatric heart transplant. Nonetheless, the study does show that excess weight is an independent risk factor for survival post-transplant. Taking into account the well-known effects of obesity and the cardiometabolic syndrome associated with severe obesity, this illustrates the urgent need for further study into the differential effect of obesity severity on outcomes and the development of practical and clinically significant weight loss interventions. Obesity is a complex phenomenon that requires a comprehensive interdisciplinary treatment approach to be effective. Despite the challenges, effective obesity management provides an opportunity to reduce its potential negative health effects. For example, in adults, mechanical support is at times viewed as a means to facilitate weight loss by providing hemodynamic stability while awaiting transplant or striving toward candidacy. Not surprisingly, obesity in children and adolescents does not usually resolve without an active, purposeful intervention. Primary care counseling and BMI surveillance have been shown to have only marginal effect on short-term weight loss. Therefore, most weight loss programs are multimodal lifestyle interventions, which involve both child and family-centered activities involving diet, physical activity, and behavioral therapies. A recent systematic review for
the US Preventative Task Force demonstrated that among 42 trials of lifestyle-based interventions to reduce excess weight (N = 6956), those with an estimated 26 hours or more of contact consistently demonstrated mean reductions in excess weight compared with usual care or other control groups after 6-12 months.\textsuperscript{10} Intervention groups showed absolute reductions in BMI z score of 0.20 or more and maintained their baseline weight, while control groups showed small increases or no change in BMI z score and gained a mean of 5-17 lbs. Although the effect size of these interventions appears small, the positive health benefits can be significant. Meanwhile, the clinical significance of the small benefit of medication use for weight loss remains unclear for pediatric populations.\textsuperscript{10} Surgical intervention may be an appropriate adjuvant to behavioral interventions in select cases under the guidance of a highly specialized pediatric obesity management team.

In summary, the limitation of this study affected the ability of the authors to draw conclusions on the effect of severe obesity but showed that being overweight or obese was an independent risk factor for mortality post-heart transplant. This highlights the importance of improving our understanding of the effects of obesity severity on the outcome in pediatric heart transplants, to appropriately risk stratify these patients at the time of transplant assessment for the purposes of improved transplant-related outcomes.

\section*{ORCID}

Emilie Jean-St-Michel\textsuperscript{1} \hspace{1cm} \hspace{1cm} \hspace{1cm} \hspace{1cm} \hspace{1cm} http://orcid.org/0000-0003-1725-2215

Emilie Jean-St-Michel\textsuperscript{1} \hspace{1cm} \hspace{1cm} \hspace{1cm} \hspace{1cm} \hspace{1cm} Alene Toulany\textsuperscript{2}

\textsuperscript{1}Division of Cardiology, The Labatt Family Heart Centre, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

\textsuperscript{2}Division of Adolescent Medicine, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

\section*{REFERENCES}


